MR48505

TSCA HEALTH & SAFETY STUDY COVER SHEET

8EHQ-0601-14941B

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1.0 SUBMISSION TYPE

8(d) **XX 8(e)** FYI 4 OTHER: Specify_____

XX- Initial Submission - Follow-up Submission Final Report Submission

Previous EPA Submission Number or Title if update or follow-up: Docket Number, if any: #

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2.1 SUMMARY/ABSTRACT ATTACHED (may be required for 8(e): optional for §4, 8(d) & FYI) X- YES NO	**2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID** 7106 4575 1292 03377852 01-2-5	**2.3 FOR EPA USE ONLY**

3.0 CHEMICAL/TEST SUBSTANCE IDENTITY

Reported Chemical Name (specify nomenclature if other than CAS name):

CAS# N/A

Purity ___%

X- Single Ingredient

Commercial/Tech Grade

Mixture *Trade Name:* BYI 11781 (Active Isomer of AMS 20234) *Common Name*: phenyllactame

CAS Number	*NAME*	*% WEIGHT*

Other chemical(s) present in tested mixture

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4.0 REPORT/STUDY TITLE

Pilot study on developmental toxicity in rats after oral administration

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5.1 STUDY/TSCATS INDEXING TERMS

[CHECK ONE]

HEALTH EFFECTS (HE):__X___ ENVIRONMENTAL EFFECTS (EE):_____ ENVIRONMENTAL FATE (EF):_____

5.2 STUDY/TSCATS INDEXING TERMS (see instructions for 4 digit codes)

STUDY TYPE:_ DTOX	SUBJECT ORGANISM (HE, EE only) RATS	ROUTE OF EXPOSURE (HE only):__	VEHICLE OF EXPOSURE (HE only)_
Other:	*Other:*	*Other:*	

6.0 REPORT/STUDY INFORMATION Study is GLP

Laboratory Bayer Toxicology Report/Study Date_5/23/01

Source of Data/Study Sponsor (if different than submitter) _____ Number of pages _-

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7.0 SUBMITTER INFORMATION

Donald W. Lamb

VP, Product Safety & Regulatory Affairs Phone: 412-777-7431

Bayer Corporation - 100 Bayer Road, Pittsburgh, PA. 15205

Submitter Address (if different): _____

Technical Contact: ___Same as above_____ Phone: ( )_____

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8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS

This compound is COMPANY SANITIZED

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Submitter Signature: Donald W Lamb **Date:** 5/25/01

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Continuation of 2.1

TSCA 8(e) Review: Effects on intrauterine development can not be completely excluded at the 150 mg/kg dose level for the marginally increased incidence of post-implantation loss, necrotic placental borders, marginally decreased placental weight, retarded ossification, marginally increased incidence of common skeletal malformations, and wavy ribs. Thus the reporting.

ABSTRACT: Seven inseminated female Wistar rats (150 mg/kg dose group had 11 rats) were treated daily by gavage from days 6 to 19 PC with 0 and 150 mg/kg of BYI 11781 (the active isomer of AMS 20234) in 0.5% aqueous carboxymethylcellulose doses . The fetuses were delivered by cesarean section on day 20 p.c. Investigations were performed on the general tolerance of the test compound by the females as well as on its effect on intrauterine development.

One female in the 150 mg/kg dose group (without implantation sites) showed increased water intake together with increased urination for one day during treatment, light colored feces at the end of treatment and enlarged kidneys at necropsy. Toxicologically relevant effects regarding feed intake and body weight development were not evident at the 150 mg/kg dose level, except for a marginal decrease in feed intake from days 6 to 9 p.c. which were near pretreatment values. This finding was comparable to recent historical control data. Necropsy revealed one female with an enlarged spleen. Toxicological relevance of these findings are equivocal, since only one female each was affected.

With respect to intrauterine development, litter size, fetal sex distribution, and fetal weight were not affected by treatment. Post-implantation loss was marginally increased at the 150 mg/kg level, yet there were no effects on the mean number of viable fetuses. Necrotic placental borders were only observed in the dosed group and mean placental weight was marginally reduced. Since both findings were within the range of historical control data, final evaluation was not possible due to the low number of females in a pilot study. Fetal external evaluation revealed one fetus with a domed head in the 150 mg/kg dose group; not confirmed as a malformation during the visceral evaluation. All together, 3 fetuses (in 3 litters) with common unspecific malformations were seen at the 150 mg/kg dose level: one fetus with interatrial septal defect of the heart (regarded as incidental based on the incidence in historical controls), one fetus with kinked scapula, and a one fetus with dysplastic sacral vertebral body. Also, a possible increase in wavy ribs (variation; at the upper range of historical control data of recent pilot studies) and retarded ossification of vertebral bodies were seen at the 150 mg/kg level. Since skeletal forelimb malformations and wavy ribs were observed at higher dose levels in a former pilot study, toxicological relevance can not be completely excluded for fetal findings in the 150 mg/kg group of the current study. A slight increase in the incidence of slight renal pelvis dilation was observed in the 150 mg/kg group as well. However, since this finding was not evident at higher dosages in a former pilot study, toxicological relevance of renal pelvis dilation was not assumed.

In summary, maternal findings were marginally evident at the 150 mg/kg dose level (increased water intake and urination for one day and light colored feces in one female; a marginal reduction in feed intake, and a alterations of the kidneys and spleen). Effects on intrauterine development can not be completely excluded at the 150 mg/kg dose level for marginally increased incidence of post-implantation loss, necrotic placental borders, marginally decreased placental weight, retarded ossification, marginally increased incidence of common skeletal malformations, and wavy ribs.